

# Behind the Breakthrough Podcast - University Health Network

## Season 5 - Dr. Gelareh Zadeh

### Transcript

**Christian** [00:00:02] Welcome. This is Dr. Geller. Is that episode September 19th for Behind the Breakthrough. Three two. Welcome to another episode of Behind The Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christian coach, with us on the podcast today. We're so pleased to have Dr. Geller Azad, a neurosurgeon, medical director of Incredible Brain Institute division, head of neurosurgery at UAH and Sprite Department of Surgery and award winning senior scientist at the Princess Margaret Cancer Centre. Dr. Zadeh is a pioneer in the research of meningioma. Take two. Dr. Zida is a pioneer in the research of meningioma or skull based tumours. Dr. Geller resigning. Welcome to Behind the Breakthrough.

**Gelareh** [00:01:00] Thank you.

**Christian** [00:01:01] Let's start with what is a meningioma?

**Gelareh** [00:01:04] Meningioma is the most common brain tumours that we see. And in fact if you remove brain cancer, meningioma is are more than 50% of the tumours that we have in our brain. They stem from the covering of the brain, the meninges, the layer that's outside of the brain matter itself. And it's an abnormal growth. It's an overgrowth of the meningeal tissue. What causes it? We don't know. There are certain conditions we know that make you prone to forming a meningioma. So, for example, childhood radiation or if you needed radiation for any reason as a child, whether it be cancer or other, that involves the skull, the brain. Then as a consequence, 10 to 15 years down the line, you're at higher risk of forming meningioma as there are genetic conditions. For example, neurofibromatosis type two that makes you prone to forming a meningioma because the abnormal gene neurofibromatosis type two results in the formation of meningioma. But otherwise, why majority of the people get random. A meningioma is not known to take too. Did I answer that? Okay, perfect. Are my pauses too long?

**Christian** [00:02:27] Not at all. No, I'm doing really well. We can always.

**Gelareh** [00:02:32] Okay.

**Christian** [00:02:33] Leading in again. Okay, so what's the scope and scale of meningioma in Canada?

**Gelareh** [00:02:39] That's a very good question. The actual incidence of meningioma, in particular the meningioma, is that we need to intervene is not exactly known because majority of the population have a small growth of a meningioma. So when they do autopsy series, many of us, almost 80% of us will have some form of a growth that's abnormal on the meninges. It's akin to having a mole on your skin. However, on occasion one of them then grows abnormally fast or over many years of slow growth. It gets to a point where then it compresses the brain and that compression results in a significant deficit. And that's how the patient becomes aware of having a meningioma or it causes an irritation to the brain and the patient has a seizure or the meningioma. There's 18 different types of meningioma. Some of them secrete material that irritates the brain and then as a consequence, that causes irritation, seizure, a deficit like a weakness of an arm or a leg or

problem with speech, problem with vision. One of the challenges with meningioma is that it can occur anywhere in the brain and the spine, but more predominantly on the brain. And it often then because it's a slow growth, in fact entangles a lot of critical neural structures. So it finds its way to wrap around cranial nerves that control all the movement of our face, our swallowing, our ability to speak, our eyesight, etc., and then starts wrapping around blood vessels that form the sheets of tumour around the blood vessel. And then, as I said, it can put pressure on the brain. And on occasion when the meningioma is an aggressive type, it can in fact invade kind of like roots inside the brain. So that becomes the challenge in that separating and teasing it away, dissecting it off microscopically, removing it away from the critical structures of the brain is where the challenge stems from for us as surgeons, but also more importantly for the patient. Because to protect the cranial structures, the nerves, the brain, the vasculature, we might then have to leave some small amounts behind. And then that layer often tends to regrow. And then we have to think of ways to be able to tackle that piece that's left behind.

**Christian** [00:05:09] It almost, almost sounds like the picture you're painting of like Medusa and her hair.

**Gelareh** [00:05:14] Some of them are. I mean, we get into the some of them are, some of them end up under the microscope. You could see that they have tentacles almost so like Medusa's hair that end up going into the brain. And so you have to tease that away without entering the brain or removing the brain, but really just pulling out each of these pieces. And as you can imagine, if they've been there for years, they've really become integrated almost as part of the brain. And so the brain is irritated upon us trying to remove it in that manner.

**Christian** [00:05:46] Just try to be. You can hear everything. That's fantastic. So what's the. Take two. So what's the prognosis for someone if they're diagnosed in time for treatment when they if they have an meningioma?

**Gelareh** [00:06:02] Majority of meningioma is are benign. They do extremely well. And we're able to remove them completely with surgery. There is a subset and again, the exact percentage isn't known, but about 15% are what we call a grade two meningioma by histopathology, because they have some of the aggressive features that I told you. And then there are about 5% that are grade three, which are extremely aggressive. They actually have a prognosis that's worse than the most malignant brain tumours. The prognosis is about 12 to 18 months in the form of a grade three meningioma. Now what we did research on is that though the histopathology grading is very important and we've relied on it for decades and guiding our decision making for the patients. We know in clinical practice that the grading is not precise. And so sometimes though, the patient's tumour is thought to be a grade one meningioma, so a benign meningioma, it acts very aggressively. And sometimes, although we think it's a grade three meningioma, the patient actually does very well with it once the tumour is resected. In the case of a grade three, we automatically used to give the patient radiation. But if it didn't behave aggressively, the question was why we irradiating unnecessarily. And that resulted in us doing a research project that wanted to look at molecular genomic mechanisms of classifying meningioma as that superseded histopathology. That would give us more clinically relevant, meaningful, precise classification schemes that we could then use in clinical practice and decision making for the patients.

**Christian** [00:07:55] So just before we drill down into your research, but in doing preparation for our conversation today, I kind of find it surprising that meningioma is not

well understood up to this point and are kind of understudied. Why is that in, say, in the industry?

**Gelareh** [00:08:12] Yeah, that's a very good question. First of all, all brain tumours are considered to be rare. If you look at the incidence of brain tumours compared to lung cancer or breast cancer or melanoma that are the more common tumour types. And so studying them becomes difficult because the numbers are smaller. Second majority of the meningioma is are benign and surgery does cure them. And so we haven't really thought about. But 30 to 40% of people who don't do well with their meningioma. But we felt that there was this void and this need and we created the Meningioma Consortium in 2016. And I'm really encouraged to see that, in fact, the field has blossomed and so many other centres across the world are now focusing on meningioma. And there's a wealth of literature being produced for us to better understand the disease, how we can classify it better, understand its behaviour better, see how we can do better with therapeutics outside of surgery. So I think the need has always been there. It was needing to identify individuals who wanted to have that focus, that interest to pursue understanding the disease. And so with that, we've actually really, I think, catalysed a movement in the field of neuropsychology, where previously majority of the research is focussed on glioblastoma, which is a deadly cancer to now understand when tumours. I think another reason is because glioblastoma, which is research that I do too right, is so deadly. Unfortunately, that majority of our attention goes to focus on glioblastoma because no subset of glioblastoma do well, unfortunately. And so majority of the funding, the focus, the efforts is on glioblastoma to try and make some headway in this disease. And then as a consequence, other brain tumours take a little bit of a backseat to glioblastoma. But I think the field is changing. And as I said, we've seen an explosion of research on meningioma, which is very good.

**Christian** [00:10:24] Okay, so let's dive into your meningioma research focusing here on the 2021 paper in Nature. Just set the scene for us here because you and your team set out to better understand. My understanding is the biology or the road map or the makeup. Sorry, of the tumour. Before we get into that, what's the importance of knowing the biology of a meningioma?

**Gelareh** [00:10:44] By knowing the biology of any tumour, you better understand how it's going to behave. You understand what's driving. It's growth. You then understand how best you can predict outcome. More importantly, are there biomarkers that distinguish my meningioma from the next person that so under the microscope they both look the same and the pathologists say their WHO grade one mine has molecular signatures that are very different from the next person. And mine says, Well, yours is about to come back sooner than the other person. And so they would be counselled differently, monitored differently, etc.. And then similarly, those same biomarkers can often provide us with avenues of treatment. And so that's very important. The ability to use those same drivers, the same genetic alterations and mutations towards a therapeutic benefit is very important and has a lot of promise. The other element of our research that I think was very exciting for us, but also obviously for the field because of the nature of the publication, no pun intended, we took a unique approach because we're at a junction where the wave of genomic data has been able to reveal signatures in all cancer types. But there's multiple ways of analysing tumours, cancers, there's methylation, there's DNA mutation, there's RNA expression sequencing, there's proteomics and in our field and to all of us as clinicians, clinicians and scientists, the question is, well, which one of these platforms is the most relevant to the patient that sits before me in clinic? Is it that I look at the mutation or do I look at what proteins are expressed? And the answer is not clear cut and depends

on which scientist and which researcher you ask. Is it the platform that's the favoured strength of one lab versus the other that's going to be the dominant? Or is the answer something beyond that? And I think that was the unique element of what we did with this cohort of tumours is that we said actually it's no one platform, it's not mutation, it's not methylation, but it's a method of where you combine these different platforms, all of this large datasets using computational methodology to then say there's four or five X number of stable subclasses of these tumours that makes clinical sense and has relevance for the patient and decision making. And so that's really what was for us a game changer in how we view meningioma is in addition to analysing them with different molecular platforms, whether it's mutation, RNA, protein, etc.. We then took another step and said, Let's take all of this data now and merge it all together till we get one clear picture that's reproducible repetitively and consistently. And that's where we get four groups of meningioma that have four distinct outcomes for very different biology and as a result, four different options for treatment. Because when you have a rare cancer rare tumour. The challenges that you then give all patients the same drug. But actually these are not the same tumours. And so the clinical trial fails after clinical trial and the field becomes dismayed and disappointed, etc..

**Christian** [00:14:26] Right.

**Gelareh** [00:14:27] So if you realise that you have actually four different subtypes of these tumours one responds to and two angiogenesis, one responds to immunotherapy, one responds to a epigenetic modifier, you then won't give the same drug to all patients. You give distinct drugs to those classes and say, Now I have the treatment for these different four classes and they are effective and you can then apply them in clinical practice.

**Christian** [00:14:57] Do you mind maybe give us a little brief synopsis then of the four classifications of meningioma that you discovered.

**Gelareh** [00:15:03] So the four classes we found, one is very angiogenic and very vascular. So they rely on vascular processes, blood vessels coming into them to help them grow. One subclass is very immunogenic, so they use a lot of immune regulatory pathways and they pull into them t cells, macrophages, all the immune cells. And the other group are very proliferative. The cells are dividing very quickly. So you could see already that these three are very distinct and the fourth group is more metabolic. It has a very unique feature. At the beginning I mentioned to you that we know meningioma is caused by a gene mutation in an F two. Well, this group we discovered has no mutation in NF to the NF two is intact, but somehow the patients form a meningioma. So again, a very novel discovery. So these four groups, then you can imagine the angiogenic group would benefit from an antiangiogenic treatment, a drug that would target the vessels. Right? The immune genic would benefit from immune therapy and the hyper proliferative the ones where the cells are dividing very fast will benefit from a drug that targets cell cycle and inhibits the cells from dividing. So that really is for us, an exciting discovery. And also, as I said, beyond just what we've shown for meningioma, it's a method to show how do we integrate the wealth of genomic data that we have in all cancer types?

**Christian** [00:16:41] And to your point about being excited by the discovery, I wanted to ask you, because, you know, now the fact you can quantify meningioma is in terms of these four classifications, kind of a gateway discovery, really. I'm curious how you reacted. To the discovery.

**Gelareh** [00:16:59] You know, I have to say, we have an active love. We have many projects ongoing. And so any time we're able to conclude a major project like this, of course, is very exciting. It's extremely rewarding. And the focus it has the attention, it gathers, the light, it shines on. That research, of course, is rewarding for us as individuals, but really more for the field because it does spark interest and it propagates that same degree of energy to try and move projects forward. Is that what you mean? Yeah. Yeah.

**Christian** [00:17:41] You didn't pop a bottle of champagne over this one.

**Gelareh** [00:17:44] I don't actually. I said, Well, yeah, No, I mean, yeah, I don't.

**Christian** [00:17:50] Okay. Picking up further in this thread, how then do you see your findings of these four classifications impacting patient treatment for meningioma now in the clinic?

**Gelareh** [00:18:01] So that's a super good question. As part of this study, we had previously shown that this one method of analysis, one of the platforms that I mentioned of the multiple platforms methylation can be used towards leveraging, creating a Sorry.

**Christian** [00:18:19] So can you try that again.

**Gelareh** [00:18:20] Yeah.

**Christian** [00:18:21] Sorry with me.

**Gelareh** [00:18:24] What word?

**Christian** [00:18:26] Oh, we need you in a get to the question with the question.

**Gelareh** [00:18:30] As part of the study leading up to this. Publication. We had discovered that if we use methylation as a mechanism to create a computational pipeline or an algorithm, we can predict the outcome of a tumour in five years. We can also predict whether a patient will respond to radiation or not. And so although we have historically traditionally used who grading by histopathology, grade one, two and three that I mentioned, we know that that's not perfect because there are some people with a who grade three meningioma that we fully respect and never have a recurrence. So it begs the question, why are we radiating them? Methylation can pull out that population. So the methylation signature allows us to determine whether a patient's going to do well or they're going to have a recurrence that supersedes overrides who classification. And so we now use that in clinical practice in decision making for our patients. Every week Monday afternoon, we have tumour board radiation oncologist, neuropsychologists and us surgeons are in the room with our allied health. Making a decision for the patient. Meningioma is resected. Do they need radiation or not? And this algorithm will determine and help us in our decision making. It took me about around two years of educating the team, convincing and demonstrating that the algorithm is actually reliable, reproducible so that it can be safely used in clinical practice. Because as you can imagine, if I withhold radiation from a patient that really needed it based on an algorithm, we've clearly not made the best decision for them. So we need a time to prospectively prove that what we've discovered is in fact, valid and safe and sensitive in detecting recurrence. And so when we completed that, we are now at a point where I don't suggest we do the methylation. My radiation oncology colleagues ask for it because they want to know, is it safe to radiate or is it necessary to radiate or not?

**Christian** [00:20:46] So further to that, then, you published your findings in the August 2021 edition of Nature. What's been the reaction of the medical community out there?

**Gelareh** [00:20:56] So in parallel to us, as I said, it's sparked interest in others as well to pursue a similar line of research. We have two other teams doing a similar approach and validating our results. And many centres from across the world then now send us their tumours for analysis to be able to detect the subclasses that I mentioned to you and give them back that algorithm of what we think the recurrence risk is. And they in turn then speak to their patient and work with them to see whether they want to go ahead with radiation, withhold radiation. And so we've ended up acting more as a referral centre on the clinical side, which is very rewarding. We need to really see how best to then make this more uniformly available to all institutions. Not all institutions do this level of genomic analysis. The method by which we can predict outcome using the algorithm is a website that's free and available for everybody to use. And so we've made that publicly available. We offer doing them methylation for them free of charge, but of course we can't do that for the whole world. So we have to be judicious and hopefully at some point we can have some mechanism where we have a cost recovery budget for it from either the ministry or other. We've been very fortunate to have philanthropy support this program because, as you could see, it sounds impactful. And so philanthropy has played a big role. In particular, our patient donors have been a huge source of support for us to be able to continue with the program.

**Christian** [00:22:46] It's fascinating that you've become this hub without without a lot of advertising, I'm guessing, for the world. Yes. Is this somehow scalable, though, that so people can start, you know, that you're more of a guide rather than doing all the diagnostics?

**Gelareh** [00:23:00] I think if we were in a different health care system, maybe in the states where there's a marketing element to what we do in health care, probably it would be scalable and would become at minimum a cost recovery exercise in our health care system, which I'm very proud of, our health care system, that's really not one of our priorities. So and to be honest, it's not my priority either. Personally, I just really want to be able to offer this to patients who ask for it themselves. And we do have. Patients are asking directly, but also practitioners who want that. And as I said, I've been very fortunate with both the institution and philanthropies supporting this work. So we've been successful in meeting the demands we have, but we really haven't marketed in it that it is something sitting there for someone who has that sort of inclination to run with it.

**Christian** [00:24:00] So what have you commercial commercialisation experts or venture capitalist?

**Gelareh** [00:24:04] They could.

**Christian** [00:24:05] There you go.

**Gelareh** [00:24:06] I mean, the question then becomes and and like I said, it's not my priority. Is there a big enough market to commercialise this? And I think there is. It's just it's. Probably not in my wheelhouse.

**Christian** [00:24:20] Let's touch on a related research. Find a yours from 2020 when you and your team published a study in Nature Medicine demonstrating the potential of a

simple blood test to diagnose and classify brain tumours. Where are you at with that today?

**Gelareh** [00:24:34] The project that we worked on was in collaboration with Daniel de Carvalho, who's a senior scientist at Princess Margaret. It was really the fortune of having such a rich environment university health network where we have a wealth of scientists, clinicians, clinicians, scientists interacting in a very seamless manner with each other through very straightforward discussions. We thought this would be an amazing opportunity to pursue his techniques and methodology to the wealth of plasma samples we have on approximately 5000 tumours. We, of course didn't analyse the 5000, but we analysed the substantial cohort and demonstrated that with 80% and higher accuracy we can diagnose based on a blood test using that methylation signature of the tumours. Different subtypes of brain tumours so we can distinguish glioblastoma wild type from IDH mutant, so totally different molecular signatures, meningioma, and others. And so that was really an impact on how we're going to be able to manage patients moving forward. And the research that's ongoing from that publication and work is to see whether in fact the blood test can tell whether you're responding to treatment in a more sensitive earlier manner than what we rely on currently, which is MRI imaging. MRI imaging, though great, has limitations because you only see the changes once the tumours reached a certain size because the sensitivity of MRI is only so much. So the blood test appears to us on the datasets that we've looked at to be able to detect recurrence much faster than MRI. And it also tells you if you're responding to a treatment or not. So that would be a game changer. It will transform what we do for our patients. And once we complete the larger dataset in our analysis, we would be ready for publishing that equally. And ultimately, the hope would be that that would get integrated into our clinical practice so that alongside an MRI test, we can then use the plasma test to more readily earlier detect a recurrence so that we can intervene sooner.

**Christian** [00:27:02] What's next for you in terms of research? What should we be on the lookout for from your lab?

**Gelareh** [00:27:06] Well, the Meningioma project continues. We're looking at the heterogeneity at a single cell level, the spatial regional alteration, but more importantly, some of the therapeutics, how it impacts the genetic make of a tumour. For the plasma test. As I mentioned, we're really focusing on the value of the test as a detector of early recurrence and response to treatment. And very recently this year, 2023, we published the results of a clinical trial that we were involved with in glioblastoma, where we use the combination of an oncolytic virus, a modified adenovirus that we inject into the centre of a glioblastoma and treat that patient with immune therapy. We have a nature medicine publication for this trial that came out May of 2023. So very, very fresh for us, very exciting, because in the process of the study we discovered that the Glioblastomas have three distinct immune signatures, one called so very low immune signature, one intermediate and one high. And the group that responds to the combination of the oncolytic virus plus immune therapy are the intermediate. The low do not respond as well. And that's likely because there isn't enough immune cells there for the immune therapy to attack. And the high don't respond as well because likely there's too much immune cells and they ward off the immune therapy. So the next step for us is to get our hands on the virus and then to be able to inject it into the tumour and take a cold tumour to a higher level of immunogenicity. And really through multiple injections of adenovirus, make it a very, very fertile ground by increasing the immune reaction in the tumour so that immune therapy can attack it. And then for the high immunogenic is to actually then not use the virus but only attack it with immune therapy. So really precision medicine for glioblastoma. Again,

glioblastoma looks the same under the microscope. They're all idea mutated. They have the same mutation pattern. But if you look at their immune signature, there's three different subtypes. So clearly not all of them are going to respond to adenovirus plus immune therapy. The cold ones probably need adenovirus, adenovirus, adenovirus multiple injections until you really rev up the tumour to become angry with the immune cells and then to attack it with immune therapy. The intermediate will respond and then the heart. Tumour microenvironment for immune cells only immunotherapy alone. So that to us is really exciting. We are in the process of trying to negotiate, to have access to the virus because this is not commercially available. But those would be the areas I would say that we're actively pursuing.

**Christian** [00:30:23] Sorry. Could you please go and shut the door? Excuse me. Still. No, it's not that. It's all right. I just like to do our show. We want you. Perfect.

**Gelareh** [00:30:38] Oh.

**Christian** [00:30:39] And you're doing a wonderful job.

**Gelareh** [00:30:40] Oh, good. Thank you.

**Christian** [00:30:41] Eliminated half my questions. Thank you. Mm hmm. Still rolling. So rolling.

**Gelareh** [00:30:49] Just to look at one thing.

**Christian** [00:30:50] Okay. Yes, we're doing well. Hmm. Check. Check. Three, two. You're listening to Behind the Breakthrough, the podcast, all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christian Coto. Today on the podcast, we're speaking with Dr. Geller Azad, a neurosurgeon, medical director of Crumble Brain Institute. Division, head of Neurology. Take two. Division, head of neurosurgery at UAH and Sprott Department of Surgery and award winning senior scientist at the Princess Margaret Cancer Centre. Dr. Zaid is a pioneer in the research of meningioma or skull based tumours and clinical translation to generate targeted therapies. Excuse me. Three, two. Galloway, You're born in Shiraz? Yes, Southwest Iran. Your father was an economist, your mother a nuclear chemist. And you were just a youngster when the Islamic Revolution of 1979 takes hold. What do you remember of life in Iran for you and your family after that?

**Gelareh** [00:32:13] We had just returned to Iran, actually, after my mom completed her studies in Oxford, in London, in England. And our plans were not firm on whether we would stay in Iran or not. But within about two weeks of us going back to Iran, the revolution happened. And I remember I didn't speak Farsi very well, but I was sitting in my grandmother's living room. My parents were out and I heard some rumbling sounds and I asked my grandmother, What do you think that was? And she said, Probably thunder. But it was a clear sunny day, so it didn't really make a lot of sense. And I realised later, of course, that they had bombed a few blocks down from where we used to live, which was close to the airport in Tehran, and that's how the war began. And we were then unable to leave Iran and we had to find ways to see whether we can safely leave. And there were various mechanisms for leaving Iran prior to the war. The way the revolution happened, there had always been episodes of unrest, perhaps in the country because it is a very socioeconomically divided country. And I think the students really created this momentum



asking for change, for equality. And that momentum was then leveraged to create this revolution that many people felt was not going to actually happen. Many people felt the Shah, the king at the time was not going to be overthrown. And I remember very clearly my dad saying to my mom, maybe we should go back to England because this looks a bit unstable. And my mom said, Who's going to overthrow the sword? Don't worry. Well, the revolution happened within about two weeks from the time the Revolutionary Guards took over the television and radio station, and the world just turned upside down. At least for me, it did. It became so disruptive and so foreign. Foreign to me. Now that I talk about it, knowing that it happened to me. But it's an out of body experience because it was such a tremendously powerful experience that I still have all the images in my head. I remember all of the things that I saw that were so shocking. And of course, I had to learn how to read and write in Farsi very quickly. I don't know how I did, but I learned it. And then I remember sitting through exams in school while the war was happening and bombs were being thrown on Tehran and the teachers telling us, you can't move. You need to sit down and write the exam and windows which sat behind me. So totally a different world from where I live in now. But, you know, I think you learn from every experience and life. You become perhaps more resilient and it opens your perspectives of where life can take you. What we have here in Canada is freedom, though of course not ever perfect. But compared to some parts of the world that it's really ideal, the set up that we have here. We then left and went back to London after some years of trying to find a way to get out of Iran. And then in London we applied for immigration to Australia and Canada. Canada responded first. We were desperate. We needed to get somewhere. We had two weeks left on our visa in London, and so we went for our Canadian interview for immigration. Mr. Murphy, who I remember very clearly in an office off Oxford Street in London, interviewed us. And because my mom's a nuclear chemist, they said, Why don't you go to Winnipeg, penalise a nuclear plant close to Winnipeg? So we ended up in Winnipeg with our very warm rain jackets on Boxing Day of 1988.

**Christian** [00:36:31] I'm laughing because I grew up in Winnipeg. Know so I know how horrible sort of I shouldn't say that how cold that was.

**Gelareh** [00:36:37] It's brutally cold. Mountains of snow were piled on top of both sides of the road. Yes, we exit the airport.

**Christian** [00:36:45] Oh, my gosh.

**Gelareh** [00:36:46] My dad says we can't live here. We're going to die. And we go back into the after.

**Christian** [00:36:51] Surviving the Iranian revolution.

**Gelareh** [00:36:53] Oh, my dad says, let's sleep here and go back tomorrow. So we did. We slept in the airport, but the next day was Boxing Day, and I didn't know then we didn't that it's the busiest day of air flight travel, so there were no planes to get. My mom said, Come on, we should just go and find someplace to live. And I didn't leave. For ten years thereafter.

**Christian** [00:37:15] You arrived in Winnipeg in 1988, and you're still a teenager.

**Gelareh** [00:37:20] Mm hmm.

**Christian** [00:37:21] For those of us who have not gone through that experience of leaving your homeland, leaving everything behind, starting over. Talk to us about the courage it takes to do that.

**Gelareh** [00:37:34] I think when you're that young, you don't look at it as courage. You just think of it as a necessity because you need to, you know, flourish. For me, I thought of it as a huge opportunity. I was so excited to have left a very oppressive system where, frankly, the war actually it was not just oppression, it was whether you were safe, whether you were going to be able to live or not, to be able to get to a place where there was so much opportunity was just an unbelievable fortune for me. What was a little bit of a shock for me is I went from London where I actually didn't go to school. I worked to Winnipeg, which at the time in 1988, 89 was a very homogeneous community society. And so I, for example, was the only immigrant to my medical school class, and I had no credentials to prove that I could go to school. So I applied. I went to schools and they said, Well, you don't have any record of going to school. We can't really accept you. But the last school that I went to, I remember it was dark. I got off the bus and I thought, I'll just go and tell my mom I tried and I didn't get into any school. I'm just going to work. I had these fantasies that I was going to work at Le Chateau. They didn't give me a job, but I walked to this law school, I think it was around 530. The counsellor was wearing her duck and to leave, I tell her my story. I must have looked sad. And she said, Okay, well, if you're telling me the truth, wear a semester school, write all the exams in January. If you pass, you can finish high school. Ms.. Gown Luck was her name.

**Christian** [00:39:19] What school?

**Gelareh** [00:39:21] Fort Richmond Collegiate.

**Christian** [00:39:22] Shout out to Fort Richmond, Centurions.

**Gelareh** [00:39:25] That's right. And I studied like mad from January 1st to January. Whatever date it was that we had to write math, chemistry, biology, etc. I did well. And then I finished high school that year.

**Christian** [00:39:41] All the better for us. Watching your parents, though, make a new life in Winnipeg and reconcile the fact they're going to stay. How does their journey shape you today?

**Gelareh** [00:39:58] Sorry. My dad had a rough week.

**Christian** [00:40:00] I'm sorry.

**Gelareh** [00:40:01] No, it's okay. I think immigration takes a lot out of people and in particular, going to a community that was so homogeneous was challenging mainly for my dad, not so much for my mom. My mom's a more flexible, malleable, joyful type person. I've never seen her upset, so she blended in more readily than my dad, who's a bit more rigorous. He has a more pronounced accent. So I think for him it was more challenging to find a position that really met his qualifications. But any job at all. At some point it was even just holding a job that became very difficult for him. So however they persisted and they were positive and encouraging for me to continue to complete my school and really made the move to give me a better future because at their stage. So Iran was not ideal for them. Their set up was much better than coming to a foreign country, an unknown place where we really had no relatives or friends. And so. Watching that, perhaps both

consciously and subconsciously, really gave me the opportunity to see what resilience is in practice and really knowing that you do need to be flexible, you need to be malleable, you need to be open to new ideas and opportunities. You need to make friends and really have them support you through any stage of your life that you do need the support system around you. And most importantly, though, being able to rely on yourself. That's a lesson I think probably shared commonly amongst first generation immigrants, where you don't go into a massive support system, you then become very reliant on your own skill sets, your own resourcefulness and your personality is shaped as a result of it. I think the flexibility and the ability to then adapt to your environment to me was a key important lesson. I don't know if you want to tape this, but I'll tell you a funny story. I get accepted to the high school and I wear my winter jacket that I bought at Sears, 50% off surf, but I thought it was really cold. And I called every day to school throwing for Richmond Collegiate this school open. The lady would say, Yes. Why? I said, Well, it's so cold outside. She said, No school is open. I did this for two weeks every day in a row and. I don't know who the lady was that answered the phone, but lesser. She never said, Why do you keep calling me? Just come to school every day. I called. They're like, Why do you ask? I'm like, It's very cold outside. Then I realise these people just go to school no matter what the weather is, because into her and if it's snow is just a scarf. Schools are closed, buses are shut down. Everybody gets a day off. So.

**Christian** [00:43:13] Winnipeggers are resilient.

**Gelareh** [00:43:15] That's right. They are. Winnipeggers are really true to the car plate friendly people. I can tell Summers from Winnipeg. They're genuinely nice people. Not that the rest of the world doesn't, but honestly, I think the car plate is correct. It's friendly. Manitoba.

**Christian** [00:43:31] We're going there to let Winnipeg know they should become subscribers to the show. Another aspect of the immigrant journey and excuse me, take to another aspect of the immigrant. Take three. Another aspect of the immigrant journey, especially for the children of immigrants such as yourself, is your your parents made a sacrifice in coming here and giving you an opportunity. Does that put pressure on you over time?

**Gelareh** [00:43:58] I don't think it puts pressure on me over time. I think, first of all, it's different for every person. You can't generalise an immigrant's experience. I think it's the opportunity that you see that was taken away and you didn't have it before. And having that opportunity and for me thinking that I'm not going to take advantage of it was what motivated me. My parents never made me feel that they did this for me or put any pressure on me or guilt in any way. I knew that that's what they did. It was not stated, but understood. But they never brought this up to me or they never kind of put it in my face or put pressured me for it. I think it was more that I thought all of these opportunities, all of these avenues that are open for me to pursue, combined with a bit of a naivete that you have as youth, you have all this positive energy. You haven't been jaded by failures. And so I thought I could really do whatever I wanted. But of course, I can't do whatever I want. I think that was a big motivating factor for me. I have to say the Society of Canada and the way it's set up again, perhaps to some it's not ideal, but it's very accepting, very welcoming, and opportunities are made available Where I'm certain had I moved to another country, I'm not sure that I would have actually had these opportunities available to me. I received a lot of scholarships for my scholastic achievements that helped me. We weren't well in terms of finances, and so I think the scholarships were really a significant positive that, again, some countries don't offer that, though civilised, they don't. And it

really made a difference for me to be able to pursue university or not at certain point where both my parents were unable to find employment. If I didn't get, for example, the Canada scholarship, I really probably wouldn't have pursued school to the level I did.

**Christian** [00:46:11] Let's turn to your come to science moment that because I understand when you were in high school, your first dream was perhaps to be an architect. Then at the University of Manitoba, that morphed into wanting to be a math professor or an engineer and then sort of an aha moment for you. Talk, talk to us about what brought you to medicine.

**Gelareh** [00:46:32] I really thought I was going to be a mathematician. And I went into actuarial math at University of Manitoba. In fact, they opened this new program for actuarial mathematics, and I think there was only 14 of us in second year. There was a course that you had to take to be able to progress in the program, And I really struggled with it. And then I struggled with myself as to whether I drop it or not, because that would change my path significantly. But me and the professor did not jive, and I now know it wasn't a personal issue. I just didn't really get the content and her style of teaching. I now know in hindsight that probably she didn't quite understand it and it wasn't making sense to me. So after days of lamenting as to whether I should drop the course, not drop the course, and my mom said, Stop talking to me about it, just make a decision. I dropped the course and then I went and mopped in some corridor somewhere. I think it was this. A tunnel. It was called the wind tunnel where you study the University of Manitoba. I was the main figure there. And randomly I bumped into two guys who went to high school. I only went to high school for that six months at Fort Richmond. I knew them, but not well, so they must've saw that I was looking sad and miserable. They came and sat with me. I tell them my version of what happened and they said, Why don't you write the M can and go into medicine? And I said, But I've not taken biology. I don't have any knowledge of anything on the market. But they said, Well, you should write it. You should go to medicine. So that's how I went into medicine. I wrote them Cat. In fact, after the first portion of I'm Cat, that day I went home for lunch. Who? You used to get a lunch break. I told my mom I'm not going back. I probably failed. She said. But we paid all this money for a year to finish it. I said, It doesn't matter. We're going to lose the money anyways because I failed. And then she encouraged me after lunch to finish them. Cat and I go on to.

**Christian** [00:48:38] Amazing at its core.

**Gelareh** [00:48:40] So it's not a very fantastic aha moment.

**Christian** [00:48:44] Sometimes it's this is also perhaps what we learn through the podcast is sometimes science is about serendipity. Yes. And there must be a connection for you when you reflect now today, because really in its essence, health care or the practice of medicine is about service being in the service of others. What's your sense of how that evolved for you, what that connection is of being in the service of others?

**Gelareh** [00:49:05] So there was always this other part of me that went into medicine really for the service of others, for taking care of patients. Again, in my naivete as a young person, I genuinely had that as my only and primary focus for doing medicine. I had no other expectation of doing science, of doing research, of advancing the field. None at all. And the same person who encouraged me to go into medical school and write the AMA cat subsequently in medical school encouraged me to do a Ph.D. and. I listen to this person and I thought I should really pursue a Ph.D. when I do my neurosurgery, because

that would be a language that I learned from molecular biology that can help me understand disease processes. And that's how I went into the scientific aspect of what I do as a physician. But neurosurgery itself is a fascinating field because we have the option of making a difference for an individual with our hands, for their skills and expertise. But also, it's a field that really still has a lot of unknowns. Neurosciences in general, our brain is an entity that we still understand very little as to why and how it degenerates, how it develops disease, and how we can regenerate and rebuild it. Unlike, for example, joints where we have a more mature understanding. So that nature of neurosciences leads us to be more inquisitive. And then as a consequence, our discoveries are impactful and really has this huge opportunity for us to be able to pursue research questions that we have in the fields that we focus on in clinical care, to then be able to define the forefront and be at the frontier of what we do in the field.

**Christian** [00:51:04] Talk to us about the role of mentors, what their role in terms of compressing your learning, shaping where you are today, in terms of your success.

**Gelareh** [00:51:14] I give majority of the positive experiences. I've had credit to the fortune of having great mentors, and I really think you find mentors yourself as an individual. You have to seek them. You have to find people who you're aligned with. You're like minded, you're similar in principles, but also for every aspect of your life. You need a different mentor, and at every stage of your life, you need a different mentor. And so across the path of my training, my education, my career, and currently I have a lot of different mentors that have been fantastic for a particular reason that I really sought their help and wanted their support, leaning on them and being able to get from them the support that I needed. I think it's an art to actually being a mentee as well. I think a good mentee needs to be open to taking direction, to having an open mind, to building that relationship. It's a form of relationship like any other that you have to trust. If a mentor gives me advice, I have to accept it. Otherwise, there's no point in actually asking for someone's advice. I then have to act on it. It doesn't mean that you blindly accept. But you then have to execute on the recommendation of that mentor to be able to really push yourself to the next limit. It might not be comfortable. It might not be something that sits well with me. But if I'm asking somebody to provide that sort of guidance to me and I trust them, then it's that I trust them to do the next step. And it might be difficult, but that's what catapults you forward at certain stages. It's tough to find a mentor because you've become so, so specialised, so focussed, so nice on what you do. But there's always people around. At this stage in my life, I think my mentors are my students. I turn to them to help me keep me up to date, really keep me energised and to keep me thinking because it's easy when you get into a truck like mine too, then a lot of what I do is routine. A lot of what I do for a patient is a standard that I want to bring to them for the care that we give. And my trainees are the ones who now say to me, not verbally, but want me to show them how do you get to that level? And so the tables turned, but I think the roles are still the same, and they teach me what the modern day demands are and what the modern day needs are for them to become the next person in their career and in their path. So that's like a full cycle for me and it's really very rewarding. And I love the ability to work with such young people that I then through them feel like I'm young, but I think they know that I'm not and probably laugh inside.

**Christian** [00:54:15] You're an incredibly impactful role model today. Thank you ever more so I would say then when you were appointed the chair of neurosurgery at the University of Toronto in 2020, you're the first woman ever in Canada to lead a university neurologic neurosurgical program. What did that mean to you?

**Gelareh** [00:54:35] When I met Jim Ruddock, who was the chair at the time that I had started my Ph.D., his charisma, thoughtfulness, skills, recognition internationally impressed me and I wanted to have his position. It wasn't with the view that I actually thought as a female I would have that impact because I really believed at the time that I started my training that the field was going to change and more women were going to go into neurosurgery and more women are going into neurosurgery, but not at the rate I anticipated they would. So of course, then being able to take on that role and then also having that opportunity to be the first female chair was doubly or manyfold, more impactful to me. It is a big responsibility because I need to figure out many firsts myself, not having a role model or a roadmap before me. But that's not been uncommon for me in this path, and that's somewhat the attraction. The impact to be able to pave the way so that hopefully future people who come after me, whether they're female or other, see that this work, this task, this role, this position is possible beyond what people have historically looked at it.

**Christian** [00:56:06] Excuse me. Further to that. You know, the supporters are. Okay. Can I please go ahead. Excuse me. I've got a bug. It's not viral. It is.

**Gelareh** [00:56:33] I always have small muscle disease. My hands don't hurt.

**Christian** [00:56:40] That's why. That's why my wife keeps me around. Good luck getting closer. Three. To further to the excuse me further to that women neurosurgeons still only make up about 15% of the field in Canada. How do you see that gap closing?

**Gelareh** [00:57:08] The number of practising female neurosurgeons actually is still less than 6%. The number of trainees and the practising neurosurgeons is about 15%. I think the reason the pace at which I thought the change was going to happen hasn't in neurosurgery is obviously multifactorial, but it is a field that is extremely demanding of an individual's time and attention. And having a family perhaps is one of the biggest factors in commitment of time and being able to withstand a significant degree of pressure because of the stress of what we handle every day, whether it's an elective operation, discussion with patients for a difficult diagnosis or trauma emergency other. I think that's true regardless of your background, but I think culturally it's expected that women have more time at home, have more time with the children, and less help in doing that. And I think that's why the gap hasn't closed as fast in some aspects. The other piece of it is, in fact, when you do surveys and you read the literature and ask females who have an interest in neurosurgery but don't pursue the profession. It's not so much. In fact, the factor of not being able to be at home and not having time at home with your family, having children, etc., it's the lack of role models. So there are many white papers written on this, and the number one factor is, in fact, the lack of role models, availability of people having allyship, kinship, seeing themselves in another person. So all my role models, outstanding mentors, have always been men, not because I deliberately picked men, but I had no females to pick from. I have, for example, never operated with a female more senior to me. It's always been a guy I know if I really wanted a female role model for some of the decisions with respect to aspects of life, that perhaps it's different for men. Historically, traditionally, culturally, it is challenging. But I think the availability of role model, not only in neurosurgery and everything, of course, is important. Having that allyship, that kinship, seeing yourself in another person. And I think that's one of the challenges and that's why the change is so slow, because few of us come into the system and therefore less of us are available for being role models to the next generation.

**Christian** [01:00:06] We need to clone you. Go, Lara.

**Gelareh** [01:00:08] I don't know. I don't know. I mean, this is off the record. A lot of people don't like doing this. Whether you're a female or a male, I mean, it's it's an excessive amount of your lifetime that you put into it. And I say to the residents, we're not the only game that does this. If you're a concert pianist, you have to spend 8 hours minimum practising the piano. You will not go and listen to a pianist. If they practice an hour a day, you would not want me to operate on you. If I operate only once a week. You want me to be able to do this with my eyes closed? Almost. Of course I need my eyes open. But. And that's one of the challenges. The difficulty, I think, is there are certain cultural expectations that I need to perhaps be home more than mine does. And so finding that partner that's accepting. I could probably say this in the book, but finding a partner that's accepting and a family and a support structure that allows you really to do the work and dedicate the number of hours that it takes is part of the challenge, in my opinion. There is one thing off the record. It tends to attract people that are a little bit difficult to deal with. Just to put it mildly.

**Christian** [01:01:27] You're from Friendly Manitoba.

**Gelareh** [01:01:32] I would tell you honestly, if I had done neurosurgery here as a medical student, I don't think I would go into neurosurgery.

**Christian** [01:01:39] Really?

**Gelareh** [01:01:39] Yeah. I shouldn't say this because I'm the chair of our program.

**Christian** [01:01:42] No, this will be in there. Yeah, right. But, of course.

**Gelareh** [01:01:45] But the men in Manitoba, the Dr. Hill male, and if a CFL hockey player for Winnipeg Blue Bombers said to me, You need to go into neurosurgery. I said, I said, Sure, Dr. Hill. He said, We need more women in this field. All of us are a little.